Practical and Safe Procedures for the Preparation of the Lower Homologues of Bromoacetylene

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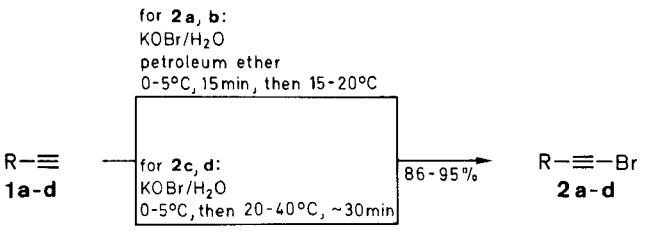
The lower homologues of bromoacetylene, from 1-bromopropyne to 1-bromo-1-hexyne, have been prepared in excellent yield by stirring the alkyne (in the cases of 1-propyne and 1-butyne a dilute solution in high-boiling petroleum ether) with a very concentrated aqueous solution of potassium hypobromite and potassium hydroxide.

Bromoalkynes **2** are important synthetic intermediates, notably in Cadiot–Chodkiewicz cross-coupling reactions leading to non-symmetrical diynes RC≡CC≡CR'.[1] As suggested by reviews[1-4] the preparation of **2** seems well established. The principal methods are reactions of a metallated alkyne, RC≡CLi or RC≡CMgBr, with bromine or a bromine-donor such as cyanogen bromide,[10] and the reaction of a free alkyne with aqueous alkali hypobromite. This reaction has already been used in 1930 by Strauss and co-workers[5] and is illustrated by an Organic Syntheses procedure[6] for bromo(phenyl)ethyne and by a number of prcedures in our laboratory manual.[7]



1, 2	a	b	c	d
R	Me	Et	Pr	Bu

Table. 1-Bromo-1-alkynes **2** Prepared

Product	Yield[a] (%)	bp (°C)/Torr	Lit. bp (°C)/Torr	n_D^{20}	Lit. n_D^{20}
2a	86	–	64[11]	1.4725	1.471[8]
2b	88	–	~50/200[9]	1.4704	1.4695[9]
2c	91	40/50	119[11]	1.4682	–
2d	95	35/12	66/50[9] 70/65[11]	1.4660	1.4657[9] 1.4666[12] (n_D^{19})

[a] Yield of isolated product **2** based on **1**.

The rate of the bromination depends upon the kinetic acidity (correlated with the pK_a value) of the alkyne and upon its water-solubility. The more acidic alkynes, 3-alken-1-ynes, 1,3-alkadiynes and arylacetylenes react smoothly, but for the complete conversion of aliphatic 1-alkynes reaction times of several hours have been reported (see e.g. Ref. 6). In some cases co-solvents or emulgators have been used. Detailed and safe experimental procedures for the lower members 1-bromopropyne (**2a**) and 1-bromo-1-butyne (**2b**) by this method are lacking. Their oxygen-sensitivity (**2a** may spontaneously ignite upon contact with air!) and the fact that propyne and 1-butyne are gases at room temperature require special experimental conditions for their preparation. In the procedures described in this communication, the use of a very concentrated aqueous solution of potassium hypobromite and an excess of potassium hydroxide enable a quick bromination of the lower homologues (up to 1-hexyne). The problem of working with gaseous acetylenes and the isolation of the oxygen-sensitive 1-bromopropyne (**2a**) has been effectively solved by using a dilute solution of these alkynes in high-boiling petroleum ether. The volatile compounds **2a** and **2b** can be isolated by warming the organic solution *in vacuo* and trapping them in a strongly cooled receiver. Monitoring of the reactions may be done by determining the refractive index of the petroleum ether solution or of the undiluted organic layer.

The preparation of the starting compounds **1** is extensively described in Ref. 7.

Caution: In view of the suspected physiological effects, the reactions and work-up should be carried out in a well-ventilated hood. 1-Bromopropyne (**1a**) may ignite upon exposure to oxygen, careful working in an atmosphere of inert gas is therefore necessary.

1-Bromo-1-alkynes; General Procedure:

For **2c,d**: KOH (90.0 g, technical quality) is dissolved in H_2O (200 mL), Br_2 (96.0 g, 0.60 mol) is added over a few min with vigorous stirring and keeping the temperature (cooling with dry ice/acetone) between 0 and −5 °C. The air in the flask is then completely replaced by N_2, after which 1-pentyne or 1-hexyne (**1c** or **1d**; 0.3 mol, 20.4 and 24.6 g, respectively) is added. The light-yellow to orange mixture is brought to 20 °C (in the case of **1c**) or 40 °C (in the case of **1d**) and subsequently agitated vigorously. During the reaction with **1c** the temperature of the mixture rises within 15 min to between 35 and 40 °C, the reaction with **1d** proceeds more slowly and the temperature may rise by a few degrees only. When the temperature begins to drop, stirring is interrupted. After some min a sample is carefully taken from the upper layer by means of a Pasteur pipette and the refractive index is determined. The mixture is stirred for an additional period of at least 30 min (depending upon the efficiency of stirring) at ca. 40 °C until the refractive index (n_D) of the upper layer has reached a constant maximal value (n_D ~ 1.467 and ~ 1.465 for **2c** and **2d**, respectively). The product is then isolated by extraction with pentane (2 × 50 mL), drying the organic solution ($MgSO_4$) and distillation (in both cases the greater part of pentane is distilled off (bath temperature ≤ 70 °C) at normal pressure under N_2). The

bromoalkynes are obtained in at least 85% yields. With the less soluble, higher homologues the reactions proceed much more slowly.

For **2a,b:** the gases **1a** or **1b** (0.4 mol, 16.0 and 21.6 g, respectively), are first dissolved in high-boiling (bp > 190 °C/760 Torr) petroleum ether (120 mL) cooled at − 20 °C. The solution of hypobromite (see above) is covered with petroleum ether (40 mL). A cold-finger filled with dry ice and acetone is placed on the flask, after which the air is completely replaced by inert gas. The mixture of petroleum ether and hypobromite solution is brought at 0 °C (in the case of **1a**) or + 5 °C (in the case of **1b**), after which the solution of the alkyne is added (from a dropping funnel) over 15 min with vigorous agitation. The temperature of the mixture rises gradually to between 15 and 20 °C. Stirring is continued after the n_D of the upper layer has reached a constant maximal value (considerably higher than the n_D of the solution of the gases in petroleum ether). The layers are then separated (in the case of the air-sensitive compound **2a** the separating funnel is first filled with inert gas!) and the organic layer transferred into a 2-L round-bottom flask containing boiling stones and ~ 10 g of $MgSO_4$. After vigorous shaking (in the case of **2a** under inert gas!) the flask is equipped for vacuum distillation: 30-cm Widmer column, condenser and single receiver cooled at − 75 °C (dry ice/acetone). The system is evacuated (water aspirator) and the flask gradually heated. When the petroleum begins to reflux in the upper part of the column, the distillation is stopped and nitrogen is admitted. After addition of a small amount of $MgSO_4$ (2–4 g) to the contents of the receiver, the procedure is repeated without external heating. A second repetition of the evacuation–condensation procedures gives the bromoalkynes in greater than 80% yields.

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